Remarks

I. Introduction

By the present Amendment, claim 30 has been amended. No claims have been added or canceled. presented for consideration. Accordingly, claims 2-15, 18-30, and 128-131 remain pending in the application. Claim 128 is independent.

II. Office Action Summary

In the Office Action of January 13, 2006, claim 30 was objected because of an informality. Claim 30 was also rejected under 35 U.S.C. §112, first paragraph as failing to comply with the enablement requirement. Claims 2-10, 13-15, 18-28, and 128-131 were rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 5,510,240 issued to Lam et al. ("Lam") in view of Zheng et al. ("Zheng"), and further in view of Bause, and still further in view of the Invitrogen catalog. Claims 11, 12, and 128 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lam in view of Zheng, and further in view of Vyas et al. ("Vyas"). Claims 19, 23, 28, 29, and 128 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lam in view of Zheng and Bause, and further in view of the Invitrogen catalog, and still further in view of Davis et al. ("Davis"). These rejections are respectfully traversed.

III. Objection to the Claims

Claim 30 was objected because of an informality. The Office Action indicates that the terms "carbohydrates" and "lipids" should be separated by a comma.

By the present Amendment, claim 30 has been amended to correct this informality. Withdrawal of the objection is therefore respectfully requested.

IV. Rejections under 35 U.S.C. §112, first paragraph

Claim 30 was rejected under 35 U.S.C. §112, first paragraph as failing to comply with the enablement requirement. Regarding this rejection, the Office Action indicates that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the relevant art to practice the invention.

As to the requirements for sustaining a rejection under 35 U.S.C. §112, first paragraph, Applicants note that the Patent Office bears the burden of presenting objective evidence to support such a rejection. Further, neither the statute nor the caselaw require a blueprint, tutorial, and/or working examples in order to satisfy the enablement requirement. Applicants need only provide a specification that enables one skilled in the art to practice the invention defined by the claims. The mere fact that routine experimentation would be required is insufficient to allege that the disclosure is somehow not enabled. See *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 52 USPQ2d 1129, 1135-36 (Fed. Cir. 1999).

In support of this rejection, the Office Action lists eight factors to be considered for a determination of undue experimentation, as established by the CAFC in the decision of *In re Wands*. 8 USPQ2d 1400 (Fed. Cir. 1988). These factors are as follows:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability of the art, and (8) the breadth of the claims.

Regarding the first factor, the Office Action alleges that the amount of experimentation is unknown because specification does not provide guidance or examples.

At the outset, Applicants note that instant disclosure is quite clear on how the invention should be practiced. The steps recited in the claims provide sufficient guidance to a skilled artisan. The claimed invention is intended to assist a skilled artisan in reducing the time, cost, and experimentation necessary to arrive a desired result. It is not intended to teach or otherwise tutor a skilled artisan on how to conduct their own experiments.

The Office Action provides no information or evidence that would lead one to believe such results could be obtained in any other manner so as to render the routine experimentation described as part of the claimed methodology unduly burdensome. Additionally, there is no requirement for the specification to completely eliminate the need to perform a certain level of experimentation. The amount of experimentation required must be taken in context with the art to which the invention pertains. In fact, it has been held that a success rate of 1% (20 out 1746 attempts) is reasonable in the complex field of gene integration, and not illustrative of undue experimentation. See *Ex parte Chen*, 61 USPQ2d 1025, 1028 (B.P.A.I. August 22, 2001) (unpublished).

Applicants further note that the invention does not attempt to eliminate the practice of assaying. Rather, the claimed invention actually reduces the number assays necessary to identify certain culture medium components. Additionally, the claimed invention allows quicker identification of culture medium components

capable of producing a desired result, when compared to the uncertainty associated with conventional methods that involve assaying alone. A conventional experiment, for example, may necessitate assaying of a large number culture media, while the present invention would require assaying of a reduced number of culture media that accurately represents all possible culture media. In this regard, it is somewhat perplexing how performing less assays could possibly lead to an undue amount of experimentation.

The Office Action indicates, with respect to factor 2, that the specification does not present specific guidance for practicing the claimed invention.

In this sense, it appears that the Office Action is require a tutorial based on a lack of appreciation for the claimed invention. However, the Examiner's own personal requirements cannot supersede the statutory requirement that the specification is not intended to be a tutorial. The specification need only enable practice of the invention. See *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 68 USPQ2d 1940, 1944 (Fed. Cir. 2003). As noted by the Federal Circuit, "A patent is not a scientific treatise, but a document that presumes a readership skilled in the field of the invention." Emphasis added. See *Ajinomoto Co., Inc. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 56 USPQ2d 1332, 1338 (Fed. Cir. 2000). See also *Staehelin v. Secher*, 24 USPQ2d 1513, 1516 (B.P.A.I. 1992) ("The error we see in Staehelin's approach to the question before us is that Staehelin would require a patent specification to be a blueprint which, if followed, would unfailingly reproduce exactly an applicant's claimed invention. However, the law does not require a specification to be a blueprint in order to satisfy the requirement for enablement under 35 USC 112, first paragraph."). Furthermore, as discussed during previously

conducted interviews, the claimed methodology has been used to identify several peptides and/or culture media that have been patented or are currently under examination before the Patent Office.

As stated by the Federal Circuit, however, the specification need only enable practice of the invention. It is not intended to be a blueprint or tutorial, nor is it intended to provide a roadmap of every possible application with detailed results. The claimed invention is not directed to compounds whose productions are affected by the applied compounds. The claimed invention is, in fact, directed to the identification of culture media containing test compounds (e.g., peptides) to affect the production of the compounds listed in claim 30. As such, it is inappropriate to require the specification to support compounds that have yet to be identified because the invention has not been applied. The specification also presumes a skilled artisan understands the art. Consequently, a skilled artisan would understand how to apply the claimed invention to identify compounds whose production has been affected. Further, the Examiner is requiring Applicants to perform every possible experiment and identify all types of compounds whose activities can be affected by the applied culture media. This clearly contradicts what the Federal Circuit and MPEP require of the specification.

Regarding factor #3, the Office Action indicates that the specification does not present working examples of the claimed method or disclose how claimed subject matter is enabled. However, as previously discussed, there is no requirement for providing a tutorial. It is perplexing why the Examiner would assume that a skilled artisan would not be capable of measuring the ability to alter production of, for example, steroids by cultured cells. In reality, the skilled artisan is already

performing this task based on extensive experimentation. Further a skilled artisan would fully appreciate the reduction in experimentation provided by the claimed methodology. As previously discussed, the specification need only be sufficient to enable one skilled in the art to understand and practice the invention. Importantly, the Office Action makes no attempt at identifying why a working example is necessary or why a skilled artisan would be unable to practice the invention without a working example. Regarding this factor, Applicants additionally note that the burden is on the Patent Office to present evidence as to why the content of the disclosure should not be presumed as enabling. See *In re Angstadt*, 537 F.2d 498, 190 USPQ 214, 219 (C.C.P.A. 1976).

The Office Action indicates that "[t]he nature of the invention, screening of the effect of peptide libraries, is complex." However, this is precisely one of the problems that the invention addresses. Considering the complexities associated with screening for the effect of peptide libraries and culture medium components, the present invention provides an ability to significantly reduce the actual number of screenings performed while increasing the size of the culture media libraries considered. This necessarily entails a reduction of the amount of screening necessary. Thus, it would only appear reasonable that a proportional reduction in complexity would be attained.

Regarding factors 5-7, the Office Action indicates (at Item D) that Applicants do not show how the prior art serves to enable the claimed subject matter and (at item G) that Applicants to not show how the prior art supports enablement of the claimed invention. See page 5 of the Office Action.

The Examiner errs in making these statements. The prior art is not intended to enable the claimed subject matter. Rather, the specification is intended to enable the claimed invention to one skilled in the art. To this end, the instant specification is not intended to be a tutorial (as requested by the Office Action), but rather a tool to assist the skilled artisan. It is unquestionable that a skilled artisan is capable of performing tasks such as assaying and measurement of desired properties. A skilled artisan is aware of the number of assays that must be performed, and would readily appreciate the advantages (e.g., costs and time) associated with a reduction in the number of assays performed while increasing the size of the library that can be considered. Furthermore, the fact that the Office Action has failed to identify prior art related to the claimed invention, or capable of predicting usability of the claimed method, is entirely insufficient for meeting its burden of establishing a *prima facie* case of non-enablement. It is also well established that the content of the disclosure should be presumed as enabling. The lack of prior art also points to the novelty and nonobviousness of the claimed invention.

Finally, the Office Action alleges that "[t]he claims are broad in that they are drawn to a method without experimental support that shows that it can be used." Again, Applicants point to the fact that the specification is not intended to be a tutorial. Next, the breadth of the claims need only be supported by the specification. There is no requirement for experimental support where a skilled artisan is clearly capable of practicing the invention. Furthermore, as previously indicated, the instant invention has been used to successfully identify peptides and culture media having desired properties.

Applicants respectfully submit that the pending claims satisfy the requirements of 35 U.S.C. §112, first paragraph. Withdrawal of this rejection is therefore respectfully requested.

V. Rejection under 35 U.S.C. §103

Claims 2-10, 13-15, 18-28, and 128 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lam in view of Zheng, and further in view of Bause, and still further in view of the Invitrogen catalog. Regarding this rejection, the Office Action alleges that Lam discloses most of the features recited in independent claim 128. The Office Action indicates that Lam fails to show that the RPMI medium is a synthetic medium and to utilize a space-filling analysis to measure properties. Lam is also indicated as failing to show determination of parameters of the first library before screening, or determination of functions of quantitative structure activity relationships, (QSAR) analysis. The Office Action relies on the Invitrogen catalog for showing that the RPMI medium consists entirely of defined compounds, and on Zheng for disclosing a method of constructing and refining a peptide library by use of QSAR analysis. Bause is relied upon for disclosing the analysis of peptide sequences by consideration of space-filling parameters. The Office Action also provides citations to various passages where these features are allegedly disclosed.

Independent claim 128 defines a method of identifying a culture medium component that comprises the steps:

> identifying a predetermined set of test compounds;
> parameterizing the predetermined set of test compounds by determining at least one parameter for each test compound in the predetermined set of test compounds;
> performing a space-filling design of the parameterized predetermined set of test compounds to identify a plurality of first test

compounds, wherein the plurality of first test compounds is a subset of the predetermined set of test compounds;

constructing a first test library comprising a plurality of first culture media, each of which contains a respective first test compound;

determining a property, having an indicia, of the plurality of first culture media;

measuring the indicia of the property of the plurality of first culture media;

determining a quantitative relationship between the measured indicia of the property, and at least one parameter of the plurality of first test compounds;

calculating an estimated indicia for a plurality of candidate culture media using the determined quantitative relationship, wherein each candidate culture medium contains a respective candidate test compound from the predetermined set of test compounds that is not in the first test library;

setting a test requirement having a test indicia range;

selecting a second test library comprising at least one second culture medium, wherein each second culture medium is a candidate culture medium having an estimated indicia that satisfies the test requirement;

measuring the indicia of the property of the at least one second culture medium; and

identifying at least one second culture medium having a measured indicia that satisfies the test requirement.

According to the invention defined by independent claim 128, a predetermined set of test compounds is identified. A subset (i.e., smaller number) of the predetermined test compounds is then selected to be parameterized through determination of at least one parameter. The parameter can correspond to various properties of the test compounds. A space-filling design is then performed for the parameterized subset of test compounds. A first test library is constructed to include a plurality of first culture media. Each of the first culture medium contains at least one first test compound identified using the space-filling design. Furthermore, the plurality of first test compounds is a subset of the predetermined set of test compounds. Next, a quantitative relationship is derived between a measured indicia of the first culture media and at least one parameter of the first test compounds. The

indicia can reflect, under certain circumstances, a value for a desired property of the first culture media. According to one or more embodiments of the invention, the relationship can have a mathematical component capable of being applied to other (untested) culture media.

Next, an estimated indicia is calculated for a plurality of candidate culture media using the derived relationship. The candidate culture media each contain a respective candidate test compound from the predetermined set of test compounds. Furthermore, the candidate test compounds are not used in the first test library. A test requirement is set with an indicia range. The test requirement can be set based on desired properties, characteristics, or specific research being conducted. A second test library is selected to include at least one second culture medium. Each of the second culture medium corresponds to a candidate peptide having an estimated indicia that satisfies the test requirement. Next, the indicia of each second culture medium is actually measured. Second culture media having a measured indicia that satisfies the test requirement are subsequently identified.

As can be appreciated, one or more embodiments of the invention provide a candidate library that contains actual lead compounds expected to have certain desired properties. This expectation is based on the indicia calculated (or estimated) using the derived relationship. The culture media containing these lead compounds can subsequently be tested to confirm the presence of these desired properties. This can be particularly useful, for example, in situations where a high number of test compounds exist (e.g., peptide identification). It can often be expensive and time consuming to test culture media containing individual test compounds to identify those having desired properties using conventional methods. Thus, the actual

number of experiments conducted can be significantly reduced through application of the invention defined by independent claim 128.

The claimed invention can be used, in part, to reduce time and costs by predicting a subset of test compounds (from a very large library of test compounds) that will have the desired properties. Users are able to consider the use of culture media, containing a substantially large group of test compounds, that could potentially have an indicia which satisfies the test requirement. The first test library can then be filtered to a smaller candidate library. The compounds from the candidate library can be relatively diverse relative to one another, while still satisfying the test requirement. A user would then take the compounds identified in the candidate library and conduct actual experimentation to obtain more accurate values for the desired properties of the culture media.

The Office Action states that "[a] second library of compounds not present in the first library of compounds that meets a predetermined range of properties as assessed in the first screen is then constructed and screened in media. The second screen is used to select a culture medium component with desired properties." See page 6, last sentence bridging to page 7.

This statement is erroneous for two reasons. First, it misconstrues what is plainly recited in the claim. Second, it omits recited features and purports to reject the claim as a whole.

The claim clearly recites a step of "selecting a second test library comprising at least one second culture medium, wherein each second culture medium is a candidate culture medium having an estimated indicia that satisfies the test

requirement." Thus, these second culture medium are not merely selected because they meet a predetermined criteria assessed in the first screen. This also shows the omission of various claim steps including (1) determination of a quantitative relationship and (2) calculation of an estimated indicia for candidate culture media using the quantitative relationship. In fact the rejection of claims 2-10, 13-15, 18-28, and 128-131 is completely silent on how any of the cited references disclose these features. This silence is also maintained in the response to Applicants' arguments.

In the rejection, the Office Action admits that Lam fails to disclose features of the claimed invention such as: (1) the RPMI medium being a synthetic medium, (2) utilization of a space-filling analysis to measure properties, (3) determination of parameters of the first library before screening, or (4) determination of functions of quantitative structure activity relationships (QSAR) analysis. However, Lam also fails to provide any disclosure or suggestion for additional features recited in independent claim 128.

Applicants' review of Lam suggests that Lam discloses a method of screening a peptide library. Lam provides assays for biological activity of a bio-oligomer from a library treated for removing any toxic molecules remaining from synthesis. The biological activities assayed can include toxicity and killing, stimulation and growth promotion, and physiological change. As indicated in the Office Action, Lam assays random peptide libraries on beads added to cells in growth media. Lam never identifies a predetermined set of test compounds. Further, because Lam assays random peptide beads, it is not possible to clearly determine the effect of individual and/or predetermined compounds (or individual peptides).

Lam further fails to construct a first test library as set forth in the claimed invention. Lam discusses preparation of beads that are selectively cleavable from the solid-phase support. This differs from the claimed identification of a predetermined set of test compounds, particularly in view of the fact that each of the claimed test compounds can be individually tested and/or parameterized. Again, Lam does not parameterize predetermined test compounds by determining a specific parameter for each test compound. Since Lam fails to perform a space-filling design (as admitted in the Office Action), then Lam must necessarily fail to provide a library of first culture media that contain at least one first test compound identified by the space-filling design.

The Office Action alleges that Lam further provides a second round of screening where a second library is synthesized. However, as clearly stated at the cited passage in Lam, the second library is "based on the common sequences of the ligands selected during the first screening." See col. 17, lines 19-24, emphasis added. Lam appears to identify higher levels of activity by merely setting a more stringent threshold level for re-screening selected ligands identified in the first library. Lam further discusses suspension of beads in a well, and subsequent release of a peptide to exert a biological activity. Beads from wells with biological activities are then sequenced and tested to determine which particular sequence demonstrated biological activity. See col. 22, lines 20-31. Accordingly, Lam does not apply a quantitative relationship to estimate the indicia of candidate test compounds that are not in the first test library (i.e., ligands that were not screened during the first round, or beads that were not in the library).

The Office Action next alleges that Zheng discloses a method of constructing and refining a peptide library by use of QSAR analysis. Zheng is also indicated as disclosing libraries that are most likely to have a desired activity. Applicants' review of Zheng has revealed various differences from the claimed invention. Zheng discloses a method for rational design of targeted combinatorial libraries. The method seeks to select a subset of available building blocks that are most likely to be present in active compounds. For example, Zheng describes the design of a targeted library with bradykinin (BK) potentiating activity. The methodology begins with twenty eight (28) known BK potentiating pentapeptides that are used as a training set. Thus, the initial peptides are known to provide certain levels of activity. By using these initial 28 BK potentiating peptides as a training set, the representative space does not encompass the entire pentapeptide space. Further, the peptide are biased toward certain activity. Consequently, any peptides that are subsequently identified will necessarily be close in space to the 28 initial peptides, and also display similar activities.

In contrast, the claimed invention takes an unbiased approach to representing the compound space and identifying new compounds that display the desired levels of activity. This allows for the discovery of potential compounds that are far away from each other in the compound space, but still display the desired levels of activity. Furthermore, Zheng never performs various steps recited in the claimed invention. For example, Zheng never identifies a predetermined set of compounds and never performs a space-filling design to identify first test compounds that are a subset of the predetermined set of compounds and also representative of the entire space occupied by the predetermined set of test compounds. Rather, Zheng's

methodology begins with peptides known to have desired levels BK potentiating activity. At best, this corresponds to the fifth step performed in independent claim 128. Consequently, Zheng still fails to provide any disclosure or suggestion for the initial steps recited in independent claim 128, i.e.:

> identifying a predetermined set of test compounds;
> parameterizing the predetermined set of test compounds by determining at least one parameter for each test compound in the predetermined set of test compounds;
> performing a space-filling design of the parameterized predetermined set of test compounds to identify a plurality of first test compounds, wherein the plurality of first test compounds is a subset of the predetermined set of test compounds;
> constructing a first test library comprising a plurality of first culture media, each of which contains a respective first test compound;
> determining a property, having an indicia, of the plurality of first culture media;

The Office Action also indicates that Bause discloses the analysis of peptide sequences by consideration of space-filling parameters. However, Bause still fails to provide any disclosure or suggestions for the aforementioned features recited in independent claim 128. Furthermore, the claimed invention is directed to more than the use of space-filling design.

The combination of references cited in the Office Action simply fails to provide any disclosure or suggestion for all the features recited in independent claim 128 as required by the M.P.E.P., notably:

> identifying a predetermined set of test compounds;
> parameterizing the predetermined set of test compounds by determining at least one parameter for each test compound in the predetermined set of test compounds;
> performing a space-filling design of the parameterized predetermined set of test compounds to identify a plurality of first test

compounds, wherein the plurality of first test compounds is a subset of the predetermined set of test compounds;

constructing a first test library comprising a plurality of first culture media, each of which contains a respective first test compound;

determining a property, having an indicia, of the plurality of first culture media;

measuring the indicia of the property of the plurality of first culture media;

determining a quantitative relationship between the measured indicia of the property, and at least one parameter of the plurality of first test compounds;

calculating an estimated indicia for a plurality of candidate culture media using the determined quantitative relationship, wherein each candidate culture medium contains a respective candidate test compound from the predetermined set of test compounds that is not in the first test library;

setting a test requirement having a test indicia range;

selecting a second test library comprising at least one second culture medium, wherein each second culture medium is a candidate culture medium having an estimated indicia that satisfies the test requirement;

measuring the indicia of the property of the at least one second culture medium; and

identifying at least one second culture medium having a measured indicia that satisfies the test requirement.

It is therefore respectfully submitted that independent claim 128 is allowable over the art of record.

Claims 2-15, 18-30, and 129-131 depend, either directly or indirectly, from independent claim 128, and are therefore believed allowable for at least the reasons set forth above with respect to independent claim 128. In addition, these claims each introduce novel elements that independently render them patentable over the art of record.

Applicants note that the Office Action attempts to support application of Zheng by alleging that the claims "do not require unbiased samples for assay in the test library, and the first test library is explicitly claimed as biased in claim 129." While neither admitting nor denying the accuracy of this statement, it is unclear why claim 130 was not addressed since this claim explicitly recites that "the test compounds are unbiased toward any predetermined activities."

Notwithstanding the references' failure to disclose all features of the claimed invention, they do not appear to be properly combinable to support a rejection under 35 U.S.C. §103. According to the Federal Circuit and the M.P.E.P., a *prima facie* case of obviousness requires that three basic criteria be met. First, there must be some suggestion or motivation in the primary reference to modify, combine, or seek out the teachings of a secondary reference. Second, there must be a realistic expectation of success from combining the two references. Finally, the prior art references must clearly teach or suggest all the claim limitations. See M.P.E.P. §706.02(j). The Federal Circuit has consistently supported the requirements of the M.P.E.P. in stating, for example, that "[i]n proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art." *In re Fritch*, 972 F.2d 1260, 23 USPQ 2d 1780 (Fed. Cir. 1992).

In the decision of *In re Fine*, 5 USPQ 2d 1596 (Fed. Cir. 1988), the court pointed out that the PTO has the burden under '103 to establish a *prima facie* case of obviousness and can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references. As

noted by the court, whether a particular combination might be "obvious to try" is not a legitimate test of patentability and obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. The teachings of the prior art must be examined objectively, and not in view of the claimed invention. As further noted by the court, one cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.

Furthermore, such requirements have been clarified in the decision of *In re Lee*, 61 USPQ 2d 1430 (Fed. Cir. 2002) wherein the court, in reversing an obviousness rejection, indicated that deficiencies of the cited references cannot be remedied with conclusions about what is "basic knowledge" or "common knowledge". The court pointed out:

> The Examiner's conclusory statements that "the demonstration mode is just a programmable feature which can be used in many different device[s] for providing automatic introduction by adding the proper programming software" and that "another motivation would be that the automatic demonstration mode is user friendly and it functions as a tutorial" do not adequately address the issue of motivation to combine. This factual question of motivation is immaterial to patentability, and could not be resolved on subjected belief and unknown authority. It is improper, in determining whether a person of ordinary skill would have been led to this combination of references, simply to "[use] that which the inventor taught against its teacher."... Thus, the Board must not only assure that the requisite findings are made, based on evidence of record, but must also explain the reasoning by which the findings are deemed to support the agency's conclusion. (emphasis added)

In the present case, there is no motivation to combine the references. First, three of the references (namely Lam, Zheng, and Bause) are in different fields of endeavor. For example, Lam relates to peptide screening for identification and characterization of ligands. Zheng relates to medicinal chemistry and targeted

combinatorial libraries. Additionally, Zheng's methodology is directed to the discovery of compounds *in-vivo*. Bause relates to the study of structural requirements of N-glycosylation of proteins as conformational probes.

In contrast, the present invention relates to identification of medium components for pharmaceutical design, drug discovery, and identification and/or design of peptides with particular pharmacological or therapeutic activities. See abstract. According to one or more embodiments, the present invention is useful for identifying culture medium components and for pairing new culture medium components with established media components. The present invention can also be used to identify compounds with desired activities for use in culture medium, drug discovery and therapy, as well as diagnostics. See page 5, lines 4 – 7 and 18 – 20. According to one or more embodiments, media formulated by the present invention can result in improved products for diagnostic applications such as plated media, dehydrated culture media, liquid media, and/or new formulas to enhance manufacturing of products in fermenters and bioreactors, as well as media for cell research and drug discovery. See page 5, line 29 – page 6, line 4. according to at least one embodiment, the present invention can be used to identify compounds for use as a component of cell culture medium, tissue culture medium, or organ culture medium. See page 17, lines 6 – 19. Further, the present invention can be used to find peptides capable of altering cell growth, proliferation, maturation, or differentiation of cultured cells. See original claim 27. This particular capability is useful for stem and progenitor cell cultures. The present invention can also be used to alter peptide or protein production in cultured cells, which is useful in the manufacture of drugs and vaccines. See original claim 28.

It is not clear why a skilled artisan working to identify and characterize ligands (as Lam discloses) would seek out the teachings of Zheng, which relate to targeted combinatorial libraries, for purposes of modifying their system. It is an even further stretch for a skilled artisan to additionally seek out the teachings of Bause, which relate to proline peptides as conformational probes. Even if the teachings of Zheng and Bause were sought, it is not clear how, or why, one working to identify and characterize ligands would suddenly derive a method for identifying medium components by reading these three references without the benefit of hindsight. There is simply no realistic expectation of success from combining these three references.

Even if the references were properly combinable, and this is a very far stretch, they would still fail to suggest the invention defined by independent claim 128. As previously discussed, Lam fails to disclose specific features of the claimed invention, including derivation of a quantitative relationship and application of such a relationship to estimate the indicia of candidate culture media. While Bause discusses a space-filling model of a particular hexapeptide, such a model does not appear to correspond to a space-filling design that is intended to represent, for example, a peptide/compound space. Rather, it appears to be a three-dimensional structure of the peptide which identifies potential sugar-attachment sites. Notwithstanding these shortcomings, there is simply no suggestion or motivation to combine the two references to arrive at the claimed steps. The combination of references simply fails to disclose or suggest the combination of features recited in the claimed invention, such as:

identifying a predetermined set of test compounds;

parameterizing the predetermined set of test compounds by determining at least one parameter for each test compound in the predetermined set of test compounds;

performing a space-filling design of the parameterized predetermined set of test compounds to identify a plurality of first test compounds, wherein the plurality of first test compounds is a subset of the predetermined set of test compounds;

constructing a first test library comprising a plurality of first culture media, each of which contains a respective first test compound;

determining a property, having an indicia, of the plurality of first culture media;

measuring the indicia of the property of the plurality of first culture media;

determining a quantitative relationship between the measured indicia of the property, and at least one parameter of the plurality of first test compounds;

calculating an estimated indicia for a plurality of candidate culture media using the determined quantitative relationship, wherein each candidate culture medium contains a respective candidate test compound from the predetermined set of test compounds that is not in the first test library;

setting a test requirement having a test indicia range;

selecting a second test library comprising at least one second culture medium, wherein each second culture medium is a candidate culture medium having an estimated indicia that satisfies the test requirement;

measuring the indicia of the property of the at least one second culture medium; and

identifying at least one second culture medium having a measured indicia that satisfies the test requirement.

Claims 11, 12, and 128 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lam in view of Zheng, and further in view of Vyas.

As previously discussed, however, Lam and Zheng both fail to provide any disclosure or suggestion for certain features recited in independent claim 128. The

inclusion of Vyas as a tertiary reference does not remedy this shortcoming, because Vyas also fails to disclose these same features.

Accordingly, independent claim 128, and dependent claims 11 and 12 are further believed allowable over the art of record.

Claims 19, 23, 28, 29, and 128 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lam in view of Zheng in view of Bause, and further in view of the Invitrogen catalog, and still further in view of Davis.

As previously discussed, however, Lam and Zheng both fail to provide any disclosure or suggestion for certain features recited in independent claim 128. The inclusion of three additional references does not remedy this shortcoming, because these references also fail to disclose these same features.

It is therefore respectfully submitted that claims 19, 23, 28, 29, and 128 are allowable over the art of record.

VI. Conclusion

For the reasons stated above, it is respectfully submitted that all of the pending claims are now in condition for allowance. Therefore, a Notice of Allowance is believed in order, and courteously solicited.

If the Examiner believes that there are any matters which can be resolved by way of either a personal or telephone interview, the Examiner is invited to contact Applicants' undersigned attorney at the number indicated below.

Authorization

Applicants request any shortage or excess in fees in connection with the filing of this paper, including extension of time fees, and for which no other form of payment is offered, be charged or credited to Deposit Account No. 01-2135 (Case: 1385.45510VX1).

Respectfully submitted,
ANTONELLI, TERRY, STOUT & KRAUS, LLP.

Leonid D. Thenor
Registration No. 39,397

LDT
1300 N. Seventeenth Street
Suite 1800
Arlington, Virginia 22209
Tel: 703-312-6600
Fax: 703-312-6666

Dated: July 26, 2007